

### **REMARKS**

Currently, claims 1, 29, 36 and 41 stand rejected under 35 U.S.C. §112, second paragraph, in regard to “substituted form” being indefinite. In response to this rejection, this phrase has been deleted from the corresponding claims and, as such, this rejection is submitted to have been overcome. Additionally, claims 1, 5-7, 29, 30, 32-36 and 38-40 stand rejected under 35 U.S.C. §103(a) over Grilli et al. (WO 98/20864) in view of Bakhshi et al. (*Journal of Neuro-Oncology*, 26, 133-9). Further, claims 4, 31, 37 and 41 stand rejected under 35 U.S.C. §103(a) over Grilli et al. and Bakhshi et al. in view of McGeer et al. (U.S. 5,192,753). New claim 42 has been added. It is submitted that no new matter has been added by way of this amendment.

#### **Remarks Directed to Rejection of Claims 1, 5-7, 29, 30, 32-36 and 38-40 under 35 U.S.C. §103(a) over Grilli et al. in View of Bakhshi et al.**

Applicant submits that the pending independent claims 1, 29 and 36 and those that depend therefrom are nonobvious over Grilli et al. in view of Bakhshi et al. on the basis that there is no reasonable expectation of success given the teachings of this prior art reference and that therefore a *prima facie* case of obviousness has not been established. In addition, it is submitted that the combination of Grilli et al. and Bakhshi et al. also does not establish a *prima facie* case of obviousness since the teachings of the Bakhshi et al. reference do not supplement the teaching lacking in Grilli et al.

Grilli et al. is cited as teaching “the treatment of Alzheimer’s disease through the use of NSAIDs” (Office Action July 28, 2005, page 3) and that “neuronal damages (i.e. neurotrauma or neuronal injury) related to Alzheimer’s disease are specifically taught as treatable by the NSAIDs disclosed therein.” (Office Action July 28, 2005, page 3 citing page 6 of Grilli et al.).

It is further asserted that “cranial and spinal traumas are also taught to be treatable by the methods disclosed.” (Office Action July 28, 2005, page 3 citing page 6 of Grilli et al.).

Bakhshi et al. is cited to bolster Grilli et al. through a teaching of drug administration to the CNS for the treatment of Alzheimer’s disease via intrathecal catheter “... alleviating adverse systemic effects associated with the administration of the drug, ensure adequate blood-brain barrier penetration, etc., as taught by Bakhshi et al.” (Paper No. 20050721, page 4, paragraph 1).

The passage apparently cited by the Examiner in the Grilli et al. reference (page 6) states that “[i]t has been found that such non-steroidal anti-inflammatory compounds are particularly suitable for use in the prevention of glutamate receptor-mediated neuronal damages related to Alzheimer’s disease ... cranial and spinal traumas ...”. Applicant submits that Grilli et al. provides evidence that pretreatment of cultured cells with a non-steroidal anti-inflammatory compound protects some cells from glutamate receptor mediated injury. For example, the Grilli et al. specification details cultured cell exposure to a glutamate receptor agonist, NMDA, whereupon some cells “became acutely necrotic: they exhibited highly swollen cytoplasm containing large vacuoles, nuclear shrinkage and focal clumping of chromatin.” (Grilli et al., page 9, line 30 – page 10, line 2). The Grilli et al. specification goes on to describe that *in vitro* “application of ASA preserved hippocampal cell viability from the NMDA-mediated injury.” (Grilli et al., page 10, lines 3-5). Further experiments describe the protective effects of NSAIDs on cultured cells exposed to glutamate where “ASA and/or NaSal were added to the chamber 2 min before glutamate exposure.” (Grilli et al., page 11, lines 9-10). Thus, Grilli et al. extensively describes protection of cells using NSAIDs.

As Bakhshi et al. only teaches Alzheimer’s disease as the indication for intrathecal drug delivery, the limitations of Grilli et al. are not bolstered by Bakhshi et al. with respect to

treatment of neurotrauma as claimed. Assuming a theoretical combination treatment through the practice of Grilli et al. and Bakhshi et al., the claimed limitation of treating neurotrauma is lacking. Since this claimed limitation is lacking in the prior art, Applicant submits that it is entitled to patentable weight. As a claimed limitation is not found in the prior art reference combination, it is submitted a *prima facie* case of obviousness has not been established.

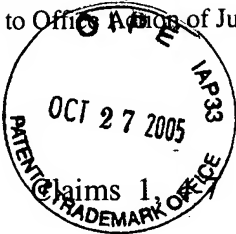
Applicant notes that the present specification and claims describe treatment of “a subject having neurotrauma.” Given the teaching of Grilli et al. and Bakhshi et al. regarding prevention of damage, Applicant submits that one of skill in the art would not have expected to have a reasonable expectation of success using an NSAID in a method including administering to a subject having neurotrauma.

In view of the above remarks, reconsideration and withdrawal of the rejection as to pending claims 1, 5-7, 29, 30, 32-36 and 38-40 under 35 U.S.C. §103(a) over Grilli et al. in view of Bakhshi et al. is solicited.

**Remarks Directed to Rejection of Claims 4, 31, 37 and 41 under 35 U.S.C. §103(a) over Grilli et al. in View of Bakhshi et al. and Further in View of McGeer et al.**

Applicant submits that this rejection is improper for the reasons detailed above. Applicant hereby incorporates by reference the above remarks with regard to the deficiencies of Bakhshi et al. McGeer et al. fails to bolster Bakhshi et al. with regard to the limitations detailed above. Additionally, claims 4, 31 and 37 are submitted to be patentable as a result of dependency from an allowable base claim.

On the basis of the above amendments and remarks, reconsideration and withdrawal of the rejection as to claims 4, 31, 37 and 41 under 35 U.S.C. §103(a) over Grilli et al. in view of Bakhshi et al. and further in view of McGeer et al. is solicited.



**Summary**

Claims 1 and 29-42 are the claims pending in this application. Each claim is believed to be in proper form and directed to allowable and patentable subject matter. Reconsideration and allowance of the claims is requested. Should the Examiner find to the contrary, he is respectfully requested to contact the undersigned attorney in charge of this application to resolve any remaining issues.

Respectfully submitted,

A handwritten signature in cursive script, reading "Avery N. Goldstein".

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A handwritten signature in cursive script, reading "Janice R. Kuehn".  
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